Approved by NIH Steering Committee 7/17/2008

Guidelines for Human Biospecimen Storage and Tracking within the NIH Intramural Research Program

Introduction

Biological specimens from patients and other study subjects must be handled according to the highest ethical and scientific standards to maintain the public's trust, to preserve and protect the specimens and the substantial investment these resources represent, and to facilitate research by maximizing use of the specimens. These guidelines set forth essential principles and practices for handling, storing, and tracking human biospecimens within the intramural research programs of the National Institutes of Health (NIH).

These guidelines complement the Guidelines for the Conduct of Research in the Intramural Research Program at NIH (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf), Standards for Clinical Research Within the NIH Intramural Research Program (http://clinicalcenter.nih.gov/ccc/clinicalresearch/index.html), Guide to Preventing Conflicts of Interest in Human Subjects Research at NIH (http://www.nihtraining.com/ohsrsite/New/COI-CR_1-4-2005FIN.pdf), and existing NIH regulations for the conduct of research such as those governing human subjects research, animal use, radiation, chemical and other safety issues, transgenic animals, and the Standards of Conduct that apply to all federal employees.

The guidelines were developed by a committee appointed by the NIH Scientific Directors and have been endorsed by the Scientific Directors and the Institute directors.

Definition of Human Biospecimens

All specimens collected by scientists in the NIH Intramural Research Program should be handled and stored following the best practices available. These guidelines apply to non-anonymized human biospecimens. Human biospecimens are biological materials defined as "including everything from subcellular structures like DNA, to cells, tissue (bone, muscle, connective tissue, and skin), organs (e.g., liver, bladder, heart, kidney), blood, gametes (sperm and ova), embryos, fetal tissue, and waste (urine, feces, sweat, hair and nail clippings, shed epithelial cells, placenta)" (Eiseman E, Castillo J, Handbook of Human Tissue Sources, RAND Monograph Report, 7, 1999). Subsets of the initial human biospecimen and derivatives of the specimens, such as extracted DNA or cell lines, that are traceable to a human subject, are considered human specimens. The guidelines apply regardless of whether the specimens were originally collected for patient care-related purposes or for research, and regardless of the subject's current vital status.

The guidelines need not apply to materials such as nucleic acids, proteins, cells, tissues, or other biological samples derived from human biospecimens that are anonymized and used as "reagents". Once human biospecimens or derivatives are put into non-human

animals, they are no longer considered human biospecimens, nor are biological inventions derived from human biospecimens.

Guidelines

To ensure proper stewardship of nonanonymized human biospecimens within the NIH intramural research programs, the Deputy Director for Intramural Research and the Scientific Directors of the NIH have endorsed the following guidelines for human biospecimen storage and tracking in relation to these topics:

1. Legal and ethical considerations
2. Collection and storage
3. Inventory database systems and tracking
4. Quality management practices including standard operating procedures
5. Shipping and sharing
6. Custodianship

1. Legal and ethical considerations

Human biospecimens used by NIH researchers must be collected, stored, used, shared, and disposed of in accordance with the informed consent signed by the subject, or under a waiver of informed consent granted by an independent ethical review body, in accordance with 45 CFR 46, Protection of Human Subjects, (http://ohsr.od.nih.gov/guidelines/45cfr46.html), as applicable and appropriate. Prospective and continuing NIH Institutional Review Board review and approval, or exemption from the NIH Office for Human Subjects Research, is required for research use of nonanonymized human biospecimens (http://ohsr.od.nih.gov/info/DDIR.html). NIH researchers must safeguard individual privacy and handle individually identifiable data in accordance with the Privacy Act (http://oma.od.nih.gov/ms/privacy/) as applicable and appropriate. Legal, ethical, and policy considerations for the collection, storage, distribution, and use of human biospecimens for research are described in detail by the Trans-NIH Bioethics Committee (Add URL, when available).

2. Collection and storage

Human biospecimens should be collected using procedures appropriate for the type of specimen being collected and its intended uses, and must be handled in accordance with the U.S. Occupational Safety and Health Administration's Bloodborne Pathogens Standard.

Human biospecimens must have an individual computer-generated label or electronic tracking device with a system-unique identifier. The identifier must enable the investigator to link to the protocol and informed consent (or waiver) under which specimen was collected, as well as the NIH Clinical Center Clinical Biomedical Translational Research Information System (BTRIS) patient identification number, as appropriate. The label must be able to withstand all potential storage conditions.

All repositories, whether large or represented by individual freezers in laboratories, should follow best practices for specimen storage and retrieval, including proper heating,

ventilation, air conditioning, lighting, security, fire protection, back-up power supplies for the facility; adequate freezer and refrigerator monitoring; back-up storage capacity; emergency preparedness plan; and maintenance and repair systems, such as those described in *Best Practices For Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research*, International Society for Biological and Environmental Repositories http://www.isber.org/Pubs/BestPractices.pdf).

3. **Inventory database systems and tracking**

Human samples obtained at NIH should be recorded in a computer-based inventory system that tracks the essential data about the specimen and its physical location. Aliquots or derivatives should be linked to the original sample. Inventory systems must meet federal requirements related to data privacy and security, such as those in the Privacy Act (http://www.usdoj.gov/oip/privstat.htm) and those issued by the National Institute for Standards and Technology (http://csrc.nist.gov/index.html), where applicable.

The inventory system should have the capacity to provide data for an annual NIH-wide assessment of storage and tracking practices, as required by the NIH Reform Act 2006. Investigators who indicate in their annual Z01 report that they work with human biospecimens must report the numbers of human biospecimens, by type of specimen, currently stored, along with information about labels and tracking systems used. Specimens collected and stored in the past year must be associated with a clinical protocol number.

Ideally, inventory systems should link biospecimens to detailed information on clinical and other variables to facilitate research, generate tracking reports, and serve as an archive so the information remains available for future use. Such data could include subject information, investigator, protocol number, sample collection time and date, specimen type, storage location, thaw counts, warnings, informed consent, clinical and epidemiologic data, assay results, and changes in custodianship. Linking specimens from NIH Clinical Center patients to their Clinical Center identification number and ultimately to BTRIS is required.

The tracking of historical collections of specimens obtained before these guidelines were issued should be upgraded to meet these guidelines when feasible. Tracking an historical collection as a single entity should be considered when entry and initiating tracking of individual specimens within an historical collection is not feasible.

4. Quality management practices including standard operating procedures

All human biospecimen collections and repositories, whether large or represented by individual freezers in laboratories, should have written standard operating procedures detailing the policies and procedures used to collect, process, handle, store, track, ship, and share biospecimens. Human biospecimens must be handled safely in accordance with OHSA regulations and recommendations, as applicable. The quality assurance

program should include periodic evaluation of adherence to the standard operating procedures.

Procedures should include an annual verification of the physical location of a random sample of the biospecimens to confirm that the appropriate biospecimens are in the correct location, as indicated by the inventory system. The sample should be large enough to detect a 0.2% error rate.

5. Shipping and sharing

Packaging and shipping of human biospecimens must conform to all applicable regulations and standards, including the U.S. Department of Transportation and International Air Transport Association standards. NIH researchers should use best practices to protect biospecimens from factors that could influence specimen integrity (i.e., temperature, humidity, light, structural quality, and spill containment) and to provide protection to workers and the environment.

NIH researchers must utilize written agreements to document shipping and sharing of human biospecimens with outside organizations for research purposes (see Policy for the Transfer of Materials from NIH Intramural Laboratories, http://www.ott.nih.gov/MTA). Various types of agreements can be used depending on the circumstances, for example, a Material Transfer Agreement (MTA) for the Transfer of Human Clinical Samples, a Clinical Trial Agreement (CTA), a memorandum of understanding, other types of collaboration agreements, or a Cooperative Research and Development Agreement (CRADA) for research collaborations with an industrial partner. Model agreements can be found at http://www.ott.nih.gov/model_agreements. Please consult with the appropriated IC Technology Development Coordinator for assistance (http://www.ott.nih.gov/tdc). Written agreements for the transfer of biospecimens to commercial laboratories for diagnostic or other routine analysis take different forms (e.g., purchase orders, contracts).

All human biospecimens received by NIH scientists originating from humans must be collected under 45 CFR 46, Protection of Human Subjects, as applicable and appropriate.

6. Custodianship

Human biospecimens obtained by NIH researchers are considered federal property and must remain in the custody of NIH unless transferred via a specific written agreement such as an MTA or a CRADA to an outside organization. The researcher is the custodian for the biospecimens, and procedures must be in place to track the transfer of specimen custodianship and informed consent information when the responsible investigator leaves NIH or needs to be changed for other reasons.

Institutes should have procedures to evaluate at least biennially when and how to discard nonanonymized specimens or make them available for sharing with other researchers if consistent with the informed consent, or through a waiver from an Institutional Review

Board, or an exemption from the NIH Office of Human Subjects Research. Investigators should follow the principles governing sharing of resources described in the Guidelines for the Conduct of Research in the Intramural Research Program at NIH (http://www1.od.nih.gov/oir/sourcebook/ethic-conduct/Conduct%20Research%206-11-07.pdf).

Conclusion

Human biospecimens are a valuable resource and are essential to the biomedical research conducted at the NIH. They must be collected, stored, tracked, and used according to the highest scientific and ethical standards. These guidelines provide a framework for NIH scientists for handling human biospecimens appropriately and maximizing their use in research.

Useful Resources

DHHS Office for Human Research Protections, http://www.hhs.gov/ohrp/

NIH Office of Human Subjects Research, http://ohsr.od.nih.gov/
45 CFR 46, Protection of Human Subjects,
http://ohsr.od.nih.gov/guidelines/45cfr46.html, Research Use of Stored Human Samples, Specimens or Data, http://ohsr.od.nih.gov/info/DDIR.html

Privacy Act, http://www.usdoj.gov/oip/privstat.htm

Legal, Ethical and Policy Framework for NIH-Supported Repositories, Trans-NIH Bioethics Committee, URL to be added when available.

Occupational Exposure to Bloodborne Pathogens Standard, U.S. Occupational Safety and Health Administration,
http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=STANDARDS&p_id=10051

Information Security Handbook: A Guide for Managers, National Institute of Standards and Technology, http://csrc.nist.gov/publications/nistpubs/800-100/SP800-100-Mar07-2007.pdf

U.S. Department of Transportation, http://hazmat.dot.gov, 49 CFR Regulation 173.134,
http://www.access.gpo.gov/nara/cfr/waisidx_04/49cfrv2_04.html

Dangerous Goods Regulations, International Air Transportation Association,
http://www.iata.org/dgr.htm

Material Transfer Agreements, Clinical Trial Agreements, Cooperative Research and Development Agreements, and Memoranda of Understanding. NIH Office of Technology Transfer, http://ott.od.nih.gov/MTA, http://ott.od.nih.gov/model_agreements

NCI Best Practices for Biospecimen Resources , National Cancer Institute, http://biospecimens.cancer.gov/global/pdfs/NCI_Best_Practices_060507.pdf

Best Practices For Repositories I: Collection, Storage and Retrieval of Human Biological Materials for Research, International Society for Biological and Environmental Repositories, http://www.isber.org/Pubs/BestPractices.pdf

International Agency for Research on Cancer, Working Group Reports, Volume 2, Common Minimal Technical Standards and Protocols for Biological Resource Centres Dedicated to Cancer Research, International Agency for Research on Cancer, 2007, http://www.iarc.fr/IARCPress/pdfs/standardsBRC/Standards_ProtocolsBRC.pdf